

# Natural Antioxidant $\alpha$ - Tocopherol in Combined Chemotherapy of Tumor

Palmina N.P., Maltseva E.L., *Emanuel* Institute of Biochemical Physics RAS, Moscow, Russia

Tumor growth is a pathology the development of which is largely determined by the intensity of lipid peroxidation (LPO) both in the tumour and in the tumour-host organs. There is a special system regulating LPO level localized in cell membranes. The main components of the system are free radicals, lipid composition, antioxidant enzymes, natural antioxidants (AOA), lipid microviscosity. In the tumor-host cells LPO control system is working similar to that in the normal state, except for the terminal stage of tumor growth, when the functioning of the system becomes very close to that in tumor membranes. Antitumor agents of different classes have the joint property to decrease the AOA level in tumor and tumor-host tissues. Antitumor effect is straightly correlated with this property of compounds. The most part of chemotherapeutic drugs are very toxic. During creation of combined schedule of tumor chemotherapy so named "classical" antitumor agents are injected at the maximal AOA level of tumor-host; antioxidants are used as adjuvant to decrease the toxicity. In our experiments we have studied the effect of combined chemotherapy by antitumor antibiotic adriamycin (AM) and natural antioxidant  $\alpha$ - tocopherol (TL) on the life span of mice with inoculated leukemia P-388. AM( 8 mg/kg) was injected to animals 3 days after inoculation of tumor cells, TL or  $\alpha$ - tocopherol-acetate (TLA) were introduced in a wide concentration range (  $10^{-16}$ - $10^{-4}$  M) 1 hour before. It was found that AM alone has increased the life span on 44% in comparison with control, 5% of animals were alive. The combined chemotherapy by AM and TL or TLA has elevated the life span up to 80% ( $10^{-4}$ ;  $10^{-10}$ - $10^{-12}$ M TL and TLA) and percentage of surviving animals up to 30%. The dependence effect from TL or TLA doses had non-linear character with two maxima and effect absence at the concentrations ( $10^{-5}$ - $10^{-7}$ M), which was typical for the substances having effect in ultra low doses. This regularities were in a straight line correlation with dose –dependence of protein kinase C (PK C) inhibition by TL. These data are in a good agreement with a number of literature data about PK C as a target of chemotherapeutic agents.